REMARKS

I. Status of the Claims

Claims 1-135 are pending in the application. Claims generic to a p53 protein and p53 gene are examined only with respect to the p53 gene. The claims are rejected, variously, under 35 U.S.C. §112, first paragraph, 35 U.S.C. §112, second paragraph, 35 U.S.C. §102, and 35 U.S.C. §103. The specific grounds for rejection, and applicants' response thereto, are discussed in detail below.

II. Formalities

The examiner has reiterated the election of species requirement. Applicants affirm their prior election of the species of a p53 gene, without traverse.

Applicants note the examiner's comments regarding the informality of the drawings. Formal drawings will be submitted upon the indication of allowable subject matter.

Applicants note the examiner's comments regarding the use of trademarks. Amendments to the specification have been provided.

III. Rejections Under 35 U.S.C. §112, First Paragraph

All of the claims have been rejected as either encompassing or specifically reciting gene therapy. Applicants traverse the rejection.

First, applicants object to the rejection on the grounds that the parent application, which has issued as U.S. Patent 5,747,469, has effectively disposed on these issues. The examiner has not pointed to any difference between the claims of the present application, and those of the parent, that would alter the enablement analysis. Thus, applicants submit that the issue of enablement is *res judicata* against the PTO by virtue of the issuance of U.S. Patent 5, 747,469.

Second, in contrast to the examiner's argument, gene therapy is not an unproved endeavor. Attached to this response are declarations from Dr. Jack Roth, submitted during the prosecution of U.S. Patent 5, 747,469. These declarations provide specific evidence of (a) a p53 gene therapy's effectiveness generally, and (b) specific successes using a combination of p53 gene therapy and DNA damaging agents. These declarations effectively rebut the examiner's unsubstantiated allegations regarding gene therapy.

And third, applicants dispute the examiner's analysis of the *Wand*'s factors. It is absolutely untrue that the instant specification provides guidance only for *in vitro* practice of the invention. In making this statement the examiner ignores a considerable portion of the specification, for example, pages 40-43 specifically contemplate and discuss therapeutic protocols. Moreover, methods and compositions for *in vivo* gene transfer and delivery of pharmaceutical agents also are described. For example, pages 30-34 describe the use of viral vectors to deliver therapeutic genes *in vivo*. Furthermore, starting at page 63, there is both a discussion of *in vivo* animal studies, and a description of a putative clinical protocol. Thus, there is no basis in the examiner's assertion that specification does not address *in vivo* embodiments.

Regarding the nature of the invention, the prior art, and the state of the art, while clearly evincing the complexities involved with gene therapy, do not suggest a lack of enablement. To the contrary, all of the limitations discussed by the examiner indicate that, while far from perfect, gene therapy is a viable endeavor. 35 U.S.C. §112, first paragraph does not require that the invention be free from limitations, only that it can be practiced by one of ordinary skill in the art.

Applicants also submit that though some experimentation may be required to apply the invention to particular clinical situations, that experimentation would not be considered undue, especially in light of the fact that considerable experimentation is considered routine in the field.

In light of the preceding comments, applicants respectfully request that the examiner reconsider and withdraw the rejection.

IV. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 6, 9-11 and 66 are rejected as indefinite. Claim 66 has been canceled. An amendment to claim 5 has been provided that corrects the perceived lack of clarity in claims 6 and 9-11. Reconsideration and withdrawal of the rejection is respectfully requested.

V. Rejection for Obviousness-Type Double Patenting

Claims 1-135 are rejected under the judicially-created doctrine of obviousness-type double-patenting as being unpatentable over claims 1-105 of U.S. Patent 5,747,469. Applicants will file a terminal disclaimer upon the withdrawal of all other grounds for rejection.

VI. Rejections Under 35 U.S.C. §102

Claim 1 is rejected under §102(a) as anticipated by either Lowe *et al.* or Clarke *et al.* Applicants respectfully traverse.

Neither reference teaches transfer of a p53 gene into cells. Lowe *et al.* discuss the use of germline cells that contain a disruption in the p53 gene. The production of these cells is not even described, but rather is listed merely as "unpublished data." However, if the p53 gene is ***disrupted*** in these cells, then the construct used to create such cells could not have included a p53 gene.

A careful review of Clarke *et al.* reveals that what is transferred is "a 2.5-kilobase (kb) fragment from within intron 1, a 5-kb fragment including exons 7-11, and a *pgk-neo* cassette [and optionally] a *pgk-tk* cassette ... at the 3' end of the genomic sequence." This is not a p53 gene, either.

Thus, neither references describes the transfer of a p53 gene into cells. The references cannot, therefore, be held to anticipate claim 1, which requires (in light of the election of species) transfer of a p53 gene.

In the interest of advancing the prosecution, applicants have clarified the claim by indicating that the transferred p53 gene produces a functional p53 polypeptide. Reconsideration and withdrawal of the rejections is respectfully requested.

VII. Rejections Under 35 U.S.C. §103

The examiner has rejected claims 2-25, 46-61, 67-82, 86, 115-124 and 127-30 over Lowe *et al.* and Clarke *et al.* in view of Tischler *et al.*, Wills *et al.* and Gregory *et al.* As discussed above, Lowe *et al.* and Clarke *et al.* do not teach transfer of the p53 gene to a cell. Tischler *et al.* fails to cure this defect, as it is cited merely for the provision of various DNA damaging agents. Wills *et al.* and Gregory *et al.*, describing adenoviral-p53 constructs, fail to address the issue of combined transfer of a p53 gene and DNA damaging agents. Thus, none of the references teaches or suggests the ***combination*** of p53 gene therapy and DNA damaging agents, as claimed.

Further, applicants direct the examiner to the following discussion, also provided in the context of an obviousness rejection, which can be found in the file history for U.S. Patent 5,747,469, the parent to this case:

> In addition, it is submitted that the rationale advanced in the final office action clearly cannot support the rejection advanced simply because ***there is not one single word in this entire discussion regarding likelihood of success for the claimed invention***. As the leading cases of *In re O'Farrell* and *In re Vaeck* indicate, likelihood success is a key element in an obviousness rejection, and without it the rejection must fail.
>
> Turning to the instant situation, applicants respectfully submit that it would have been impossible to know, *a priori*, what would happen when one combined the influence of a DNA damaging agent with p53-based gene therapy in a tumor cell. Not only could the combination have provided no added benefit, it might even have been detrimental (footnote omitted). This simply could not have been predicted. ***This is the touchstone of nonobviousness*** ....
>
> To further underscore the complete absence of predictability with respect to the instant claims, applicants point out that, at the time of filing, the literature was in a state of flux as to the potential relationship between p53 and DNA damage. For example, Kastan *et al.* (1991) describes experiments designed to help elucidate the role of p53 in response to DNA damage. As the discussion indicates, DNA damage appears to induce p53, which itself appeared to be associated with an arrest in DNA synthesis. This arrest in DNA synthesis, in turn, was hypothesized to permit the cell to an opportunity to repair any

damage to the DNA, preventing transmission of errors in the genetic code to progeny cells.

Taken at face value, this paper clearly raises the question of whether a DNA damaging agent and p53 would work ***against*** each other, given that [the] point of inducing DNA damage as part of a cancer therapy regimen is to trigger cell death. By providing an exogenous p53 to treated cells, one would have to consider the possibility that this would, in fat, ***counteract*** the DNA damage that had been induced, thereby canceling out the therapeutic effect. Tishler, the only reference cited by the examiner that even addresses this issue, simply confirms Kastan *et al.* in showing that DNA damage increases p53 levels. ***It does not, however, address the inherent conflict between the cell's desire to repair DNA damage and the clinician's desire to have that damage result in cell death.*** This conflict only would be exacerbated by the further provision of an exogenous p53 to a tumor cell. Thus, on its face, the teaching of Tishler ***raises*** more questions than it answers.

To further obscure the situation surrounding the interaction between p53 and DNA damage, one must turn to the 1993 paper by Stichenmeyer *et al.* This paper reports on the effect of a p53-associated G_1 checkpoint, lost in cells [that] have defective p53 function, on sensitivity to DNA damage. As stated by the authors, their "results indicate that although the cell cycle checkpoint in G_1 can be impaired through mutation of *p53* or by other mechanisms, [the] loss [of] the G_1 checkpoint *per se* does not influence radiosensitivity or sensitivity to camptothecin." Thus, this paper would lead one to the conclusion that the presence of p53 is not a critical factor in the response of a cell to DNA damage, much less that p53 could ***cooperate*** with a DNA damaging agent to produce an enhanced therapeutic effect.

Thus, in conclusion, a fair reading of the prior art (including Tishler) could not, as of applicants' filing date, have provided any reasonable inference, much less a specific suggestion, that a combination of p53 gene therapy and a DNA damaging agent would be a worthwhile endeavor in the treatment of cancer. Without such an expectation, a *prima facie* case of obviousness cannot exist ....

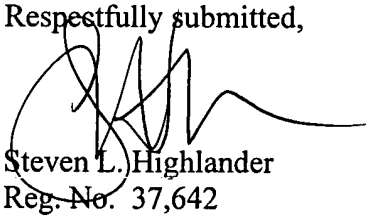
Transitional response filed December 6, 1996 (emphasis in original). Applicants are attaching copies of the Kastan *et al.* and Stichenmeyer *et al.* papers. This explanation provides a clear indication of why, even assuming one could combine the references cited by the examiner, one of skill in the art would not find the present invention "obvious."

Reconsideration and withdrawal of the rejection is respectfully requested.

VIII. Summary

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. Should Examiner Sandals have any questions regarding this response, he is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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Date: August 27, 1999

PENDING CLAIMS

1. (Amended) A method of [killing] reducing the growth rate of a cell, comprising contacting [a] said cell with (a) a [p53 protein or] gene encoding a functional p53 protein and (b) a DNA damaging agent in a combined amount effective to kill said cell.

2. (Amended) The method of claim 1, wherein said cell is contacted with [a p53 protein or] said gene in combination with X-ray radiation, UV-irradiation, γ-irradiation, microwaves, adriamycin, 5-fluorouracil, etoposide, camptothecin, actinomycin-D, mytomycin C, or cisplatin.

3. (Amended) The method of claim 2, wherein said cell is contacted with [a p53 protein or] said gene in combination with cisplatin.

4. (Twice amended) The method of claim 1, wherein said cell is contacted with a recombinant[, non-viral] vector that expresses a functional p53 protein in said cell in combination with a DNA damaging agent.

5. (Twice amended) The method of claim 4, wherein said p53-expressing recombinant, non-viral vector is a naked DNA plasmid or a plasmid within a liposome, a retroviral vector, an AAV vector, or a recombinant adenoviral vector.

6. The method of claim 5, wherein said p53-expressing recombinant vector is a recombinant adenoviral vector.

7. (Twice amended) The method of claim 4, wherein said p53-expressing recombinant[, non-viral] vector comprises a p53 expression region positioned under the control of a constitutive promoter.

8. (Twice amended) The method of claim 4, wherein said recombinant[, non-viral] vector comprises a p53 expression region, the cytomegalovirus IE promoter and the SV40 early polyadenylation signal.

9. The method of claim 6, wherein at least one gene essential for adenovirus replication is deleted from said adenovirus vector construct and the p53 expression region is introduced in its place.

10. The method of claim 9, wherein the E1A and E1B regions of the adenovirus vector are deleted and the p53 expression region is introduced in their place.

11. The method of claim 6, wherein said recombinant adenoviral vector is present within a recombinant adenovirus.

12. (Amended) The method of claim 1, wherein said cell is first contacted with [a p53 protein or] said gene and is subsequently contacted with [a] said DNA damaging agent.

13. (Amended) The method of claim 1, wherein said cell is first contacted with [a] said DNA damaging agent and is subsequently contacted with [a p53 protein or] said gene.

14. (Amended) The method of claim 1, wherein said cell is simultaneously contacted with [a p53 protein or] said gene and [a] said DNA damaging agent.

15. (Amended) The method of claim 1, wherein said cell is contacted with a first composition comprising [a p53 protein or] said gene and a second composition comprising [a] said DNA damaging agent.

16. The method of claim 15, wherein said first or second composition is dispersed in a pharmacologically acceptable formulation.

17. (Amended) The method of claim 1, wherein said cell is contacted with a single composition comprising [a p53 protein or] said gene in combination with [a] said DNA damaging agent.

18. The method of claim 17, wherein said composition is dispersed in a pharmacologically acceptable formulation.

19. (Amended) The method of claim 17, wherein said cell is contacted with a single composition comprising a recombinant vector that expresses p53 in said cell in combination with [a] said DNA damaging agent.

20. (Amended) The method of claim 19, wherein said cell is contacted with a single composition comprising a recombinant adenovirus containing a recombinant vector that expresses p53 in said cell in combination with [a] said DNA damaging agent.

21. The method of claim 1, wherein said cell is a tumor cell.

22. (Amended) The method of claim [1], wherein said tumor cell is a malignant cell.

23. (Amended) The method of claim 22, wherein said malignant cell is a lung cancer cell.

24. (Amended) The method of claim 22, wherein said malignant cell is a breast cancer cell.

25. (Amended) The method of claim 22, wherein said malignant cell has a mutation in a p53 gene.

26. (Twice amended) The method of claim 21, wherein said tumor cell is located within an animal at a tumor site [and said p53 protein or gene and DNA damaging agent are administered to the animal in a pharmacologically acceptable form].

27. (Canceled) A method of treating cancer, comprising administering to an animal with cancer a therapeutically effective combination of a p53 protein or gene and a DNA damaging agent.

28. (Canceled) The method of claim 27, comprising injecting into a tumor site a therapeutically effective amount of a pharmaceutical composition comprising a recombinant vector that expresses p53 in a tumor cell, and contacting the tumor with a DNA damaging agent.

29. (Canceled) The method of claim 28, wherein the tumor is contacted with a DNA damaging agent by irradiating the tumor site with X-ray radiation, UV-irradiation, γ-irradiation or microwaves.

30. (Canceled) The method of claim 28, wherein the tumor is contacted with a DNA damaging agent by administering to the animal a therapeutically effective amount of a pharmaceutical composition comprising a DNA damaging compound.

31. (Canceled) The method of claim 28, wherein the DNA damaging compound is cisplatin.

32. (Amended) A composition comprising a [p53 protein or] gene <u>encoding a functional p53 polypeptide</u> in combination with a DNA damaging agent.

33. (Amended) The composition of claim 32, comprising [a p53 protein or] <u>said</u> gene in combination with adriamycin, 5-fluorouracil, etoposide, camptothecin, actimomycin-D, mitomycin C, or cisplatin.

34. (Amended) The composition of claim 33, comprising [a p53 protein or] <u>said</u> gene in combination with cisplatin.

35. (Amended) The composition of claim 32, comprising a recombinant vector that expresses a <u>functional</u> p53 protein in an animal cell in combination with a DNA damaging agent.

36. The composition of claim 35, wherein said recombinant vector is a naked DNA plasmid or a plasmid within a liposome.

37. The composition of claim 36, wherein said recombinant vector is a recombinant adenoviral vector.

38. The composition of claim 37, wherein said recombinant vector is a recombinant adenoviral vector is present within a recombinant adenovirus particle.

39. The composition of claim 32, comprising a recombinant adenoviral vector present within a recombinant adenovirus particle in combination with cisplatin.

40. The composition of claim 32, dispersed in a pharmacologically acceptable formulation.

41. The composition of claim 40, formulated for intralesional administration.

42. (Amended) A therapeutic kit comprising, in suitable container means, a pharmaceutical formulation of a recombinant vector that expresses a functional p53 protein in an animal cell and a pharmaceutical formulation of a DNA damaging agent.

43. The kit of claim 42, wherein said recombinant vector and said DNA damaging agent are present within a single container means.

44. The kit of claim 42, wherein said recombinant vector and said DNA damaging agent are present within distinct container means.

45. The kit of claim 42, comprising a pharmaceutical formulation of a recombinant adenovirus including a recombinant vector that expresses a p53 protein in an animal cell and a pharmaceutical formulation of cisplatin.

46. The method of claim 21, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with X-ray radiation, UV-irradiation, γ-irradiation or microwaves.

47. The method of claim 46, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with X-ray radiation.

48. The method of claim 46, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with UV-irradiation.

49. The method of claim 46, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with γ-irradiation.

50. The method of claim 46, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with microwaves.

51. The method claim 21, wherein the tumor cell is contacted with a pharmaceutical composition comprising a DNA damaging compound.

52. The method of claim 51, wherein the DNA damaging agent is cisplatin.

53. The method of claim 51, wherein the DNA damaging agent is doxorubicin.

54. The method of claim 51, wherein the DNA damaging agent is etoposide.

55. The method of claim 51, wherein the DNA damaging agent is verapamil.

56. The method of claim 51, wherein the DNA damaging agent is podophyllotoxin.

57. The method of claim 51, wherein the DNA damaging agent is 5-FU.

58. The method of claim 51, wherein the DNA damaging agent is actinomycin-D.

59. The method of claim 51, wherein the DNA damaging agent is adriamycin.

60. The method of claim 51, wherein the DNA damaging agent is camptothecin.

61. The method of claim 51, wherein the DNA damaging agent is mitomycin C.

62. (Canceled) The method of claim 27, wherein a tumor site is contacted with a DNA damaging agent by irradiating the tumor site with X-ray radiation.

63. (Canceled) The method of claim 27, wherein a tumor site is contacted with a DNA damaging agent by irradiating the tumor site with UV-irradiation.

64. (Canceled) The method of claim 27, wherein a tumor site is contacted with a DNA damaging agent by irradiating the tumor site with γ-irradiation.

65. (Canceled) The method of claim 27, wherein a tumor site is contacted with a DNA damaging agent by irradiating the tumor site with microwaves.

66. (Canceled) The method claim 21, wherein the tumor cell is contacted with a DNA damaging agent by administering to the animal a pharmaceutical composition comprising a DNA damaging compound.

67. (Canceled) The method of claim 21, wherein the DNA damaging agent is cisplatin.

68. (Canceled) The method of claim 21, wherein the DNA damaging agent is doxorubicin.

69. (Canceled) The method of claim 21, wherein the DNA damaging agent is etoposide.

70. (Canceled) The method of claim 21, wherein the DNA damaging agent is verapamil.

71. (Canceled) The method of claim 21, wherein the DNA damaging agent is podophyllotoxin.

72. (Canceled) The method of claim 21, wherein the DNA damaging agent is 5-FU.

73. (Canceled) The method of claim 21, wherein the DNA damaging agent is actinomycin-D.

74. (Canceled) The method of claim 21, wherein the DNA damaging agent is adriamycin.

75. (Canceled) The method of claim 21, wherein the DNA damaging agent is camptothecin.

76. (Canceled) The method of claim 21, wherein the DNA damaging agent is mitomycin C.

77. (Amended) The method of claim 4, wherein said [vector] gene is administered prior to said DNA damaging agent.

78. (Amended) The method of claim 4, wherein said [vector] gene is administered after said DNA damaging agent.

79. (Amended) The method of claim 4, wherein said [vector] gene is administered at the same time as said DNA damaging agent.

80. (Canceled) The method of claim 28, wherein said vector is administered prior to said DNA damaging agent.

81. (Canceled) The method of claim 28, wherein said vector is administered after said DNA damaging agent.

82. (Canceled) The method of claim 28, wherein said vector is administered at the same time as said DNA damaging agent.

83. (Amended) The method of claim [28] 26, wherein said [vector] gene is delivered endoscopically, intravenously, intratracheally, intralesionally, percutaneously or subcutaneously.

84. (Amended) The method of claim [28] 26, wherein said tumor site is a resected tumor bed.

85. (Amended) The method of claim [28] 26, wherein said administration is repeated.

86. (Amended) The method of claim [81] 13, wherein the period between administration of the DNA damaging agent and [vector] gene is between 12 and 24 hours.

87. (Amended) The method of claim [81] 13, wherein the period between administration of the DNA damaging agent and [vector] gene is between 6 and 12 hours.

88. (Amended) The method of claim [81] 13, wherein the period between administration of the DNA damaging agent and [vector] gene is about 12 hours.

89. (Amended) The method of claim [80] 12, wherein the period between administration of the [vector] gene and DNA damaging agent is between 12 and 24 hours.

90. (Amended) The method of claim [80] 12, wherein the period between administration of the vector and DNA damaging agent is between 6 and 12 hours.

91. (Amended) The method of claim [80] 12, wherein the period between administration of the vector and DNA damaging agent is about 12 hours.

92. (Canceled) The method of claim 28, wherein said vector is delivered endoscopically, intravenously, intratracheally, intralesionally, percutaneously or subcutaneously.

93. (Canceled) The method of claim 26, wherein said tumor site is a resected tumor bed.

94. (Canceled) The method of claim 27, wherein said administering is repeated.

95. (Canceled) The method of claim 28, wherein said tumor cell is a lung cancer cell.

96. (Amended) The method of claim [28] 21, wherein said tumor cell is an epithelial tumor cell.

97. (Amended) The method of claim [95] 23, wherein said lung cancer cell is non-small cell lung carcinoma cell.

98. The method of claim 97, wherein said non-small cell lung carcinoma cell is a sqamous carcinoma cell.

99. The method of claim 97, wherein said non-small cell lung carcinoma cell is an adenocarcinoma cell.

100. The method of claim 97, wherein said non-small cell lung carcinoma cell is a large-cell undifferentiated carcinoma cell.

101. The method of claim 95, wherein said lung cancer cell is a small cell lung carcinoma cell.

102. (Canceled) The method of claim 28, wherein said tumor cell is a breast cancer cell.

103. (Canceled) The method of claim 27, wherein said cancer is a lung cancer.

104. (Canceled) The method of claim 27, wherein said cancer is an epithelial cancer.

105. (Canceled) The method of claim 103, wherein said lung cancer is a non-small cell lung carcinoma cancer.

106. (Canceled) The method of claim 105, wherein said non-small cell lung carcinoma cancer is a sqamous carcinoma cancer.

107. (Canceled) The method of claim 105, wherein said non-small cell lung carcinoma cancer is an adenocarcinoma cancer.

108. (Canceled) The method of claim 105, wherein said non-small cell lung carcinoma cancer is a large-cell undifferentiated carcinoma cancer.

109. (Canceled) The method of claim 103, wherein said lung cancer is a small cell lung carcinoma cancer.

110. (Canceled) The method of claim 27, wherein said cancer is breast cancer.

111. (Amended) The method of claim [28] 26, wherein said [vector] gene is administered in about 0.1 ml.

112. (Amended) The method of claim [28] 26, wherein said [vector] gene is administered in about 10 ml.

113. (Canceled) The method of claim 28, wherein said vector is administered in about 0.1 ml.

114. (Canceled) The method of claim 28, wherein said vector is administered in about 10 ml.

115. The method of claim 52, wherein said cisplatin is administered at 20 mg/m^2.

116. The method of claim 53, wherein said doxorubicin is administered at 25-75 mg/m^2.

117. The method of claim 54, wherein said etoposide is administered at 35-50 mg/m^2.

118. The method of claim 57, wherein said 5-FU is administered at 3-15 mg/kg.

119. The method of claim 47, wherein the x-ray dosage is between 2000 and 6000 roentgens.

120. The method of claim 47, wherein the x-ray dosage is between 50 and 200 roentgens.

121. (Canceled) The method of claim 67, wherein said cisplatin is administered at 20 mg/m^2.

122. (Canceled) The method of claim 68, wherein said doxorubicin is administered at 25-75 mg/m^2.

123. (Canceled) The method of claim 69, wherein said etoposide is administered at 35-50 mg/m^2.

124. (Canceled) The method of claim 72, wherein said 5-FU is administered at 3-15 mg/kg.

125. (Canceled) The method of claim 62, wherein the x-ray dosage is between 2000 and 6000 roentgens.

126. (Canceled) The method of claim 62, wherein the x-ray dosage is between 50 and 200 roentgens.

127. (Amended) The method of claim [7] 4, wherein said promoter is a [constitutive] promoter.

128. (Amended) The method of claim [127] 7, wherein the promoter is selected from the group consisting of SV40, CMV and RSV.

129. The method of claim 128, wherein the promoter is the CMV IE promoter.

130. The method of claim 129, wherein the vector further comprises a polyadenylation signal.

131. (Canceled) The method of claim 28, wherein said p53-expressing recombinant, non-viral vector comprises a p53 expression region positioned under the control of a promoter.

132. (Canceled) The method of claim 131, wherein said promoter is a constitutive promoter.

133. (Canceled) The method of claim 132, wherein said promoter is selected from the group consisting of SV40, CMV and RSV.

134. (Canceled) The method of claim 133, wherein the promoter is the CMV IE promoter.

135. (Canceled) The method of claim 134, wherein the vector further comprises a polyadenylation signal.